REMARKS

In view of the above amendments and the following remarks, the Examiner is respectfully requested to withdraw the rejections and allow Claims 1-23, the only claims pending and currently under examination in this application.

Claims 1 and 6 have been amended to recite that the NSAID formulation is applied to the head of the host. Support for these amendments can be found in the specification, e.g., at page 6, lines 2-3. Claim 6 has also been amended to correct a minor typographical error.

As no new matter has been added by the above amendments, the Applicants respectfully request the entry thereof.

REJECTION UNDER 35 U.S.C. §102(b)

The Examiner has rejected Claims 1, 2 and 5 under 35 U.S.C. §102(b) as being anticipated by Drizen et al. (U.S. Patent No. 5,897,880).

It is well settled that to anticipate a claim, the reference must teach every element of the claim. "A claim is anticipated [under §102] only if each and every element as set forth in the claim is found...in a single prior art reference." MPEP §2131 *citing* (Verdegaal Bros. V. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)). The Applicants respectfully submit that each and every element of the rejected claims is not set forth in Drizen et al.

Independent Claim 1, and the claims that depend therefrom, have been amended to recite that the NSAID formulation is applied to the head of a host to at least ameliorate headache pain. Thus, in order to anticipate the subject claims, Drizen et al. must teach topically applying a NSAID formulation to the head of a host to at least ameliorate headache pain.

Drizen et al. teach topical compositions that may have a drug dispersed within a polymer matrix and treatments that use such topical compositions (abstract). However, Drizen et al. do not teach that these topical compositions are applied to the head of a host. Specifically, the test procedures taught in Drizen et al. that describe a particular application site teach application to (1) the facet joint areas of the cervical spine (Test Procedure 1), (2) the facet joint area on the right side of the neck (Test Procedure 2) and, (3) the facet joint areas bilaterally in the neck

region (Test Procedure III). Accordingly, nowhere in Drizen et al. is it taught to apply a NSAID formulation to the head, as recited in the subject claims.

For at least the reason that Drizen et al. fail to teach the application of a NSAID formulation to the head of a host as claimed in Claims 1, 2 and 5, Drizen et al. do not anticipate the Claims 1, 2 and 5. Accordingly, the Applicants respectfully request that this rejection be withdrawn.

Rejections under 35 U.S.C. §103(a)

Claims 1-23 have been rejected under 35 U.S.C. §103(a) as obvious over Liedtke (US 5,840,755) in view of Drizen et al. (US 5,897,880) and Brand (US 4,681,897) for the asserted reason that Liedtke discloses a method of alleviating headache pain in human subject by applying a topical carrier containing local anesthetics and analgesics to the forehead or temple of a subject in need, which, when coupled with the topical formulations disclosed in Drizen and Brand, renders the claims obvious.

The M.P.E.P. teaches at §1242 that:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, whether in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

Thus, in order for a proper *prima facie* case to be made, a combination of references must teach or suggest all of the claim limitations with a reasonable expectation of success. In other words, in order to make a proper *prima facie* case of obvious, some reasonable expectation of success is required in making a proposed modification. As will be demonstrated below, the Applicants submit that no reasonable expectation of success is presented in either the references themselves or in the knowledge generally available to one of ordinary skill in the art that would lead one to modify the references or to combine the teachings of the references to make the combination of components claimed in the instant application.

The claims of the present application are directed to methods and kits. Independent

Claims 1 and 6, and the claims that depend therefrom, have been amended to include that the NSAID formulation is applied to the head of a host. Thus, an element of each claim is a topical NSAID formulation topically applied to the head of a host in order to provide relief from headache pain. As the kits include the methods of Claim 1, the subject kits also recite all of the limitations of Claim 1.

Lietdke discloses a composition for the topical therapy of headaches. The composition contains a local anesthetic, specifically an anesthetic having amide or ester groups, which may be applied to the forehead or temples or both (abstract; col. 2, lines 35-67). However, Lietdke does not teach or suggest compositions that include a NSAID. In fact, nowhere in the disclosure of Lietdke is the term "NSAID" even mentioned. Accordingly, Lietdke does not teach or suggest applying a NSAID formulation to a host, let alone applying a NSAID formulation to the head of a host, as claimed in the subject claims.

As described above, Drizen et al. teach NSAID formulations, but do not teach or suggest applying such NSAID formulations to the head of a host, as claimed in the subject claims, and instead specifically teach the application of NSAID formulations to the facet joint areas.

Brand discloses compositions that include capsaicin or an analog thereof and a NSAID drug. However, not only does Brand fail to teach or suggest the use of such compositions to treat headache pain, Brand also fails to teach or suggest the topical administration of the compositions to the head of a subject for the treatment of any disorder.

Accordingly, the combination of references fails to teach or suggest the application of a NSAID to the head to treat headache pain. Furthermore, modifying the references or the combining the teachings of the references to make the combination of components claimed in the instant application fails to provide a reasonable expectation of success.

Most illnesses cannot be adequately treated by simply changing the method of application of a formulation. Many formulations are known in the art that are efficient and/or effective at therapeutically relieving an illness by a particular method, but which are inefficient and/or ineffective when applied by a different method. Headache is not exceptional as an illness in this respect. In fact, because so little is known about how headaches are caused and the mechanisms by which drugs successfully treat headaches, their experimental treatment has an extremely variable level of success. Treatments and the methods of administering treatments for headaches

are largely empirically determined, and typically a low expectation of success is predicted for a particular composition and method and treatment for a headache.

The expectation of success is further lowered if the therapeutic agent is topically administered, i.e., with little or no systemic activity, as opposed to administered via a different mode. A variety of factors determine whether a drug topically applied will be effective at treating a particular illness such as a headache. For example, it is well known that simply changing the route of administration of a therapeutic agent, e.g., from oral to topical, may prove ineffective and/or inefficient. One important variable in this regard relates to the dosage required for a particular route. Accordingly, topical administration of a drug could result in an insufficiently absorbed amount of the agent such that topical administration would not be effective, or the amount of the drug that may be required to be effective when administered topically may be too great, e.g., may be toxic or produce adverse effects.

Further adding to this low expectation of success is the fact that certain topical drugs may be applied on certain parts of a body and not on others, e.g., some areas of the body may be intolerable to a particular drug or the dosage of a drug that would be necessary to treat a particular illness would be to great for a particular area. Specifically, topical drugs typically need to be topically administered at a location most effective for the particular pain being treated, however, there are locations on a host's body that may not be able to tolerate certain topically applied drugs and/or do not allow sufficient absorption of drug and thus the expectation of success is further lowered when administering a drug at a different site on the body and particularly a different region of the body such as from the truck to the head. For example, many topically applied drugs are contraindicated for areas of and about mucous membranes such as the eyes, mouth, etc., and/or areas of sensitive skin such as areas where the stratum corneum is relatively thin such as the face, but may be used with success on other parts of the body such as the torso, etc. Furthermore, the effective dose of a particular agent administered to one location may be different from the effective dose for the same agent administered to another location, e.g., due to the skin thickness at the different sites. However, changing dosages to accommodate different locations on a body may prove unsuccessful, e.g., the dosage may be too high, e.g., may be toxic, or may be too low, e.g., when lowering a dosage to accommodate sensitive skin areas.

Furthermore, even in those instances where a therapeutic agent may be administered at

various areas on the body without causing adverse reactions or intolerable side effects, the therapeutic agent may not be as effective when applied at some areas as compared to others. This may be particularly true when a therapeutic agent is applied to an area of the body wherein the agent must cross a bone barrier to be effective such as the head. Thus, the same expectation of success cannot be predicted from the application of a particular therapeutic agent to an area that does not include bone barriers and the application to an area that does include bone barriers. In fact, typically a lowered expectation of success can be predicted for a formulation that has to cross bone barriers.

In summary, some drugs produce desirable results upon topical administration whereas others do not. Furthermore, some drugs produce desirable results upon topical administration to certain areas of the body, but may be ineffective, or even produce undesirable results, when administered to other areas of the body.

Although diclofenac gel has been successful at treating some headaches when topically applied to the facet joint area, the expectation of success of an NSAID topically applied to the head to treat the same headache is very low. In fact, topical application of NSAID at facet joint area is most likely only treating one uncommon headache condition, cervicogenic headache, and will have no effect on more common headache conditions, such as tension-type headache and migraine headache, whereas topical NSAID treatment when applied to the forehead and/or temples will be able to alleviate tension-type headache and migraine headache in certain individual sufferers and will unlikely treat patients with cervicogenic headache. Although the combination of the references suggested by the Examiner may suggest that it would be *obvious to try* using a NSAID formulation on an area of the head to treat headache pain, there is certainly no prediction that the treatment would be so successful, especially in terms of the relative sensitivity of the head, as well as in terms of effectively crossing the bone barrier of the head, such that one would have a reasonable expectation of success. Since a reasonable expectation of success is not taught in the combined references, at least this prong of the three prong test of *prima facie* obviousness has also not been met and a proper prima facie case of obviousness cannot be sustained. Accordingly, the cited combination of references fails to make the claims obvious because (1) the combination of references fails to teach or suggest application of a NSAID to the head to treat headache pain, and (2) the combination of references fails to provide

a reasonable expectation of success. As such, the Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

In view of the above amendments and remarks, this application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issuance. The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, Order No. CALD-007.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: 3.4.03

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